

We Claim:

1. A method for identifying agents which may be potentially pro-apoptotic or anti-apoptotic, comprising:
 - A) providing a reaction mixture including complexes of BAK and/or M11L proteins;
 - B) contacting the reaction mixture with one or more test agents;
 - C) determining if the test agent possesses at least one of the following abilities:
 - 1) binding to the complex;
 - 2) increasing or decreasing the steady state level of the complex;
 - 3) affecting an enzymatic activity of the complex;
 - 4) affecting a subcellular localization of the complex.
2. The method of claim 1, wherein the agent is polypeptides, nucleic acids, carbohydrates, small organic molecules, or natural product extract libraries.
3. The method of claim 2, wherein the agent is from natural product extract libraries isolated from animals, plants, fungus, or microbes.
4. The method of claim 1, wherein the method is repeated for a variegated library of at least 10 different members.
5. The method of claim 4, wherein the method is repeated for a variegated library of at least 100 different members.
6. The method of claim 5, wherein the method is repeated for a variegated library of at least 1,000 different members.
7. The method of claim 6, wherein the method is repeated for a variegated library of at least 10,000 different members.
8. The method of claim 1, further comprising:
 - D) determining if the test agent, which possesses at least one of the abilities of C), is pro-apoptotic or anti-apoptotic.
9. The method of 8, wherein step D) is carried out *in vivo* or in whole cells.
10. The method of claim 1, wherein the reaction mixture is a cell-free system.

11. The method of claim 10, wherein the cell-free system comprises reconstituted protein mixture of semi-purified proteins.
12. The method of claim 10, wherein the cell-free system comprises reconstituted protein mixture of highly-purified proteins substantially lacking impurity.
13. The method of claim 10, wherein at least one member of said complexes of BAK and/or M11L proteins, or the test agent, is immobilized on a solid support.
14. The method of claim 13, wherein the immobilization is effected by chemical cross-linking, by indirect conjugating via an intermediate molecule, or by direct coating of said solid support.
15. The method of claim 14, wherein the intermediate molecule is an antibody or biotin.
16. The method of claim 13, wherein the solid support is microtiter plates, microarrays, test tubes, microcentrifuge tubes, or solid matrices.
17. The method of claim 13, wherein said at least one member of said complexes of BAK and/or M11L proteins, or said test agent is a fusion protein adapted to bind said solid support.
18. The method of claim 10, wherein at least one member of said complexes of BAK and/or M11L proteins, or the test agent, is labeled.
19. The method of claim 18, wherein the label is a radioisotope, a fluorescent label/tag, an epitope tag, or an enzyme.
20. The method of claim 10, wherein the cell-free system is generated from lysates, each containing one or more of the relevant polypeptides, which lysates are mixed appropriately or spiked, wherein no single lysate contains all the component necessary for generating said cell-free system.
21. The method of claim 20, wherein one or more of said relevant polypeptides is recombinantly generated.
22. The method of claim 20, wherein said lysates derive from one or more cell types selected from bacteria cells, yeast cells, worm cells, insect cells, amphibian cells, plant cells, or mammalian cells.

23. The method of claim 1 or 8, wherein the reaction mixture is a cell.
24. The method of claim 23, wherein the method is carried out using a yeast two-hybrid assay or reverse yeast two-hybrid assay.
25. The method of claim 24, wherein the method employs an Interaction Trap System (ITS) or reverse ITS.
26. A method of conducting a drug discovery business comprising:
 - A) providing one or more assay systems for identifying agents by their ability to inhibit or potentiate BAK-dependent and/or M11L-dependent apoptosis;
 - B) conducting therapeutic profiling of agents identified in step A), or further analogs thereof, for efficacy and toxicity in animals; and
 - C) formulating a pharmaceutical preparation including one or more agents identified in step (B) as having an acceptable therapeutic profile.
27. The method of claim 26, further comprising a step of establishing a distribution system for distributing the pharmaceutical preparation for sale.
28. The method of claim 26, further comprising a step of establishing a sales group for marketing the pharmaceutical preparation.
29. A method of conducting a target discovery business comprising:
 - A) providing one or more assay systems for identifying agents by their ability to inhibit or potentiate BAK-dependent and/or M11L-dependent apoptosis;
 - B) (optionally) conducting therapeutic profiling of agents identified in step A) for efficacy and toxicity in animals; and
 - C) licensing, to a third party, the rights for further drug development and/or sales for agents identified in step A), or analogs thereof.
30. A method to identify M11L-interacting polypeptides, comprising:
 - A) contacting M11L with a reaction mixture;
 - B) retrieving M11L, together with any M11L-interacting polypeptides, from the reaction mixture;
 - C) identifying M11L-interacting polypeptides of B) using mass spectrometry.
31. The method of claim 30, wherein M11L is a recombinant protein.

REPORT